Chimeric antigen receptor T-cell therapy remains effective after exposure to bispecific antibodies. Comment to "Sequencing of cellular therapy and bispecific antibodies for the management of diffuse large B-cell lymphoma"

In the October issue of *Haematologica*, Melody and Gordon provided a comprehensive review of sequential immunotherapies in patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL). The authors claim that the efficacy of chimeric antigen receptor (CAR) T-cell therapy in patients previously exposed to bispecific antibodies (BsAb) is currently unknown.[1] However, we recently reported the efficacy and safety of CD19 CAR T cells in patients with R/R LBCL previously exposed to CD20/CD3 or CD22/CD3 BsAb.[2] Relatively speaking, the mechanisms of action of BsAb and CAR T cells are quite similar, and this has raised concerns about potential resistance to immune-killing after progression to BsAb, along with T-cell exhaustion that could affect subsequent CAR T-cell results.[3] However, our results are reassuring. Out of 47 patients, we found that the overall response rate (ORR) and complete response rate (CRR) after CAR T-cell therapy were 85% and 43%, respectively. The 1-year progression-free survival (PFS) and overall survival (OS) were 42% and 55%, respectively. After propensity score matching analysis, we found that there was similar efficacy between patients who had been exposed to BsAb and those who were BsAb-naïve. Furthermore, CAR T-cell efficacy was similar between BsAb-resistant and BsAb-sensitive patients. Finally, we found no cross-toxicities between BsAb and CAR T cells.[2]

To date, under current approval, CAR T cells are usually given before BsAb in R/R LBCL patients. However, several ongoing trials are evaluating CD20/CD3 BsAb as part of first-line therapy in LBCL patients. If these trials are positive, in the future, BsAb may be given upfront, and thus most R/R LBCL patients will have been previously exposed to BsAb. Our study, although preliminary, suggests that prior exposure to BsAb may not preclude CAR T-cell efficacy in LBCL. The absence of cross-resistance between CD19 CAR T cells and BsAb targeting different antigens in this population does not favor a particular sequence over another.

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Contributions

Both authors wrote the comment.

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